ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

AZOPT 10 mg/ml eye drops, suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of suspension contains 10 mg brinzolamide.

Excipients: benzalkonium chloride 0.15 mg, (see section 4.4).

For a full list of excipients, (see section 6.1).

3. PHARMACEUTICAL FORM

Eye drops, suspension .

Azopt is a white to off-white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AZOPT is indicated to decrease elevated intraocular pressure in:
- ocular hypertension
- open-angle glaucoma

as monotherapy in patients unresponsive to beta-blockers or in patients in whom beta-blockers are contraindicated, or as adjunctive therapy to beta-blockers or prostaglandin analogues (see section 5.1).

4.2 Posology and method of administration

When used as monotherapy or adjunctive therapy, the dose is one drop of AZOPT in the conjunctival sac of the affected eye(s) twice daily. Some patients may have a better response with one drop three times a day.

Nasolacrimal occlusion or gently closing the eyelid after instillation is recommended. This may reduce the systemic absorption of medicinal products administered via the ocular route and result in a decrease in systemic side effects.

When substituting another ophthalmic antiglaucoma agent with AZOPT, discontinue the other agent and start the following day with AZOPT.

If more than one topical ophthalmic medicinal product is being used, the medicines must be administered at least 5 minutes apart.

Shake well before use. To prevent contamination of the dropper tip and suspension, care must be taken not to touch the eyelids, surrounding areas or other surfaces with the dropper tip of the bottle. Keep the bottle tightly closed when not in use.

Use in elderly
No dosage alteration in elderly patients is necessary.

Use in children
The efficacy and safety of AZOPT in patients below the age of 18 have not been established and its use is not recommended in these patients. However, there is limited experience in children.
The safety and efficacy of AZOPT have been studied in a small number of paediatric patients less than 6 years of age (see also 4.4, 4.8 and 5.1).

Use in hepatic and renal impairment
AZOPT has not been studied in patients with hepatic impairment and is therefore not recommended in such patients.

AZOPT has not been studied in patients with severe renal impairment (creatinine clearance < 30 ml/min) or in patients with hyperchloraemic acidosis. Since brinzolamide and its main metabolite are excreted predominantly by the kidney, AZOPT is therefore contra-indicated in such patients (see also 4.3).

4.3 Contra-indications

- Hypersensitivity to brinzolamide or any of the excipients.
- Known hypersensitivity to sulphonamides (see also 4.4).
- Severe renal impairment.
- Hyperchloraemic acidosis (see also 4.2).

4.4 Special warnings and special precautions for use

AZOPT is a sulphonamide inhibitor of carbonic anhydrase and, although administered topically, is absorbed systemically. Acid-base disturbances have been reported with oral carbonic anhydrase inhibitors. Brinzolamide has not been studied in pre-term infants (less than 36 weeks gestational age) or those less than 1 week of age. Patients with significant renal tubular immaturity or abnormalities should only receive brinzolamide after careful consideration of the risk benefit balance because of the possible risk of metabolic acidosis. The same types of undesirable effects that are attributable to sulphonamides may occur with topical administration. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation.

There is a potential for an additive effect on the known systemic effects of carbonic anhydrase inhibition in patients receiving an oral carbonic anhydrase inhibitor and AZOPT. The concomitant administration of AZOPT and oral carbonic anhydrase inhibitors has not been studied and is not recommended.

There is limited experience with AZOPT in the treatment of patients with pseudoexfoliative glaucoma or pigmentary glaucoma.
AZOPT was primarily evaluated in concomitant administration with timolol during adjunctive glaucoma therapy. Additionally the IOP-reducing effect of Azopt as adjunctive therapy to the prostaglandin analogue travoprost has been studied. No long term data are available on the use of AZOPT as adjunctive therapy to travoprost.(see section 5.1)

AZOPT has not been studied in patients with narrow-angle glaucoma.

The possible role of brinzolamide on corneal endothelial function has not been investigated in patients with compromised corneas (particularly in patients with low endothelial cell count). Specifically, patients wearing contact lenses have not been studied and careful monitoring of these patients when using brinzolamide is recommended, since carbonic anhydrase inhibitors may affect corneal hydration and wearing contact lenses might increase the risk for the cornea. Likewise, in other cases of compromised corneas such as patients with diabetes mellitus, careful monitoring is recommended.

Benzalkonium chloride, which is commonly used as a preservative in ophthalmic products, has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Since AZOPT contains benzalkonium chloride, close monitoring is required with frequent or prolonged use in dry eye patients, or in conditions where the cornea is compromised.

AZOPT has not been studied in patients wearing contact lenses. AZOPT contains the preservative benzalkonium chloride which may cause eye irritation. Benzalkonium chloride may be absorbed by soft contact lenses and is known to discolour soft contact lenses. Therefore, patients must be instructed to wait 15 minutes after instillation of AZOPT before inserting contact lenses. AZOPT must not be administered while wearing contact lenses.

Potential rebound effects following cessation of treatment with AZOPT have not been studied; the IOP-lowering effect is expected to last for 5-7 days.

Oral carbonic anhydrase inhibitors may impair the ability to perform tasks requiring mental alertness and/or physical coordination in elderly patients. AZOPT is absorbed systemically and therefore this may occur with topical administration.

4.5 Interaction with other medicinal products and other forms of interaction

Specific interaction studies with other medicinal products have not been performed with AZOPT. In clinical studies, AZOPT was used concomitantly with prostaglandin analogues and timolol ophthalmic preparations without evidence of adverse interactions. Association between AZOPT and miotics or adrenergic agonists has not been evaluated during adjunctive glaucoma therapy.

AZOPT is a carbonic anhydrase inhibitor and, although administered topically, is absorbed systemically. Acid-base disturbances have been reported with oral carbonic anhydrase inhibitors. The potential for interactions must be considered in patients receiving AZOPT.

The cytochrome P-450 isozymes responsible for metabolism of brinzolamide include CYP3A4 (main), CYP2A6, CYP2C8 and CYP2C9. It is expected that inhibitors of CYP3A4 such as ketoconazole, itraconazole, clotrimazole, ritonavir and troleandomycin will inhibit the metabolism of brinzolamide by CYP3A4. Caution is advised if CYP3A4 inhibitors are given concomitantly. However, accumulation of brinzolamide is unlikely as renal elimination is the major route. Brinzolamide is not an inhibitor of cytochrome P-450 isozymes.

4.6 Pregnancy and lactation

Pregnancy
There are no adequate data from the use of brinzolamide in pregnant women. Studies in animals have shown reproductive toxicity (see 5.3). The potential risk for humans is unknown. AZOPT should not be used during pregnancy unless clearly necessary.

Nursing mothers
It is not known whether brinzolamide is excreted in human milk, however, this substance is excreted in rat milk. It is strongly recommended to avoid the use of AZOPT when breast-feeding.

4.7 Effects on ability to drive and use machines

Temporary blurred vision or other visual disturbances, may affect the ability to drive or use machines (see also 4.8 Undesirable effects). If blurred vision occurs at instillation, the patient must wait until the vision clears before driving or using machinery.

4.8 Undesirable effects

In clinical studies involving over 1800 patients treated with AZOPT as monotherapy or adjunctive therapy to timolol maleate 5 mg/ml, the most frequently reported treatment-related adverse events were: dysgeusia (5.8%) (bitter or unusual taste, see description below) and temporary blurred vision (5.8%) upon instillation, lasting from a few seconds to a few minutes (see also 4.7 Effects on ability to drive and use machines).

The following undesirable effects were assessed to be treatment-related and are classified according to the following convention: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1000), or very rare (<1/10,000). Within each frequency grouping, undesirable effects are presented in decreasing order of seriousness.

Cardiac disorders:
Uncommon: cardio-respiratory distress, angina pectoris, bradycardia, heart rate irregular

Blood and lymphatic system disorders:
Uncommon: red blood cell count decreased, blood chloride increased

Nervous system disorders:
Common: dysgeusia, headache
Uncommon: somnolence, motor dysfunction, amnesia, memory impairment, dizziness, paraesthesia

Eye disorders:
Common: blepharitis, blurred vision, eye irritation, eye pain, dry eye, eye discharge, eye pruritus, foreign body sensation in eyes, ocular hyperaemia
Uncommon: corneal erosion, keratitis, punctate keratitis, keratopathy, deposit eye, corneal staining, corneal epithelium defect, intraocular pressure increased, optic nerve cup/disc ratio increased, corneal oedema, conjunctivitis, meibomianitis, diplopia, glare, photophobia, photopsia, visual acuity reduced, allergic conjunctivitis, pterygium, scleral pigmentation, asthenopia, ocular discomfort, abnormal sensation in eye, keratoconjunctivitis sicca, hypoaesthesia eye, subconjunctival cyst, conjunctival hyperaemia, eyelids pruritus, eyelid margin crusting, lacrimation increased

Ear and labyrinth disorders:
Uncommon: tinnitus

Respiratory, thoracic and mediastinal disorders:
Uncommon: dyspnoea, bronchial hyperactivity, cough, epistaxis, pharyngolaryngeal pain, throat irritation, nasal congestion, upper respiratory tract congestion, postnasal drip, rhinorrhoea, sneezing, nasal dryness

Gastrointestinal disorders:
Common: dry mouth
Uncommon: oesophagitis, diarrhoea, nausea, dyspepsia, upper abdominal pain, abdominal discomfort, stomach discomfort, flatulence, frequent bowel movements, gastrointestinal disorder, hypoaesthesia oral, paraesthesia oral

Renal and urinary disorders:
Uncommon: renal pain

Skin and subcutaneous tissue disorders:
Uncommon: urticaria, rash, rash maculo-papular, pruritus generalized, alopecia, skin tightness

Musculoskeletal and connective tissue disorders:
Uncommon: back pain, muscle spasms, myalgia

Infections and infestations:
Uncommon: nasopharyngitis, pharyngitis, sinusitis

Injury, poisoning and procedural complications:
Uncommon: foreign body in eye

General disorders and administrative site conditions:
Uncommon: pain, chest discomfort, asthenia, fatigue, feeling abnormal, feeling jittery, irritability

Reproductive system and breast disorders:
Uncommon: erectile dysfunction

Psychiatric disorders:
Uncommon: apathy, depression, depressed mood, libido decreased, nightmare, insomnia, nervousness

Adverse reactions identified from post-marketing experience that have not been reported previously in clinical trials with AZOPT are listed below. They are derived from spontaneous reports for which the frequency cannot be estimated. Thus, the frequency grouping is categorised as not known.

Cardiac disorders: arrhythmia, palpitations, tachycardia, hypertension, blood pressure increased, heart rate increased

Nervous system disorders: tremor, hypoaesthesia, ageusia

Eye disorders: corneal epithelium disorder, corneal disorder, visual disturbance, eye swelling, eye allergy, madarosis, eyelid disorder, eyelid oedema, erythema of eyelid

Ear and labyrinth disorders: vertigo

Respiratory, thoracic and mediastinal disorders: asthma

Gastrointestinal disorders: vomiting

Renal and urinary disorders: pollakiuria

Skin and subcutaneous tissue disorders: dermatitis, erythema

Musculoskeletal and connective tissue disorders: arthralgia, pain in extremity

Infections and infestations: rhinitis

General disorders and administration site conditions: chest pain, peripheral edema, malaise, medication residue

Immune system disorders: hypersensitivity

Hepatobiliary disorders: liver function test abnormal

In small short-term clinical trials, approximately 12.5% of paediatric patients were observed to experience drug related adverse effects, the majority of which were local, nonserious ocular effects such as conjunctival hyperaemia, eye irritation, eye discharge, and lacrimation increased (see section 5.1).

Dysgeusia (bitter or unusual taste in the mouth following instillation) was the most frequently reported systemic undesirable effect associated with the use of AZOPT during clinical studies. It is likely caused by passage of the eye drops in the nasopharynx via the nasolacrimal canal. Nasolacrimal occlusion or gently closing the eyelid after instillation may help reduce the incidence of this effect (see also 4.2 Posology and method of administration).

AZOPT is a sulphonamide inhibitor of carbonic anhydrase with systemic absorption. Gastrointestinal, nervous system, haematological, renal and metabolic effects are generally associated with systemic carbonic anhydrase inhibitors. The same type of undesirable effects that are attributable to oral carbonic anhydrase inhibitors may occur with topical administration.

No unexpected adverse events have been observed with AZOPT when used as adjunctive therapy to travoprost. The adverse events seen with the adjunctive therapy have been observed with each active substance alone.

4.9 Overdose

No case of overdose has been reported.

Treatment should be symptomatic and supportive. Electrolyte imbalance, development of an acidotic state, and possible nervous system effects may occur. Serum electrolyte levels (particularly potassium) and blood pH levels must be monitored.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Antiglaucoma preparations and miotics, carbonic anhydrase inhibitors.

ATC code: S01EC

Carbonic anhydrase (CA) is an enzyme found in many tissues of the body, including the eye. Carbonic anhydrase catalyses the reversible reaction involving the hydration of carbon dioxide and the dehydration of carbonic acid.

Inhibition of carbonic anhydrase in the ciliary processes of the eye decreases aqueous humour secretion, presumably by slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. The result is a reduction in intraocular pressure (IOP) which is a major risk factor in the pathogenesis of optic nerve damage and glaucomatous visual field loss. Brinzolamide, an inhibitor of carbonic anhydrase II (CA-II), the predominant iso-enzyme in the eye, with an *in vitro* IC_{50} of 3.2 nM and a K_i of 0.13 nM against CA-II.

The IOP-reducing effect of AZOPT as adjunctive therapy to the prostaglandin analogue travoprost was studied. Following a 4 week run-in with travoprost, patients with an IOP ≥19 mmHg were randomized to receive added treatment with brinzolamide or timolol. An additional decrease in mean diurnal IOP of 3.2 to 3.4 mmHg for the brinzolamide group and 3.2 to 4.2 mmHg for the timolol group were observed. There was an overall higher incidence of non-serious ocular adverse events, mainly related to signs of local irritation, in the brinzolamide/travoprost groups. The events were mild and did not affect the overall discontinuation rates in the studies (see section 4.8).

A clinical trial was conducted with AZOPT in 32 paediatric patients less than 6 years of age, diagnosed with glaucoma or ocular hypertension. Some patients were naive to IOP therapy whilst others were on other IOP-lowering medicinal product(s). Those who had been on previous IOP medicinal products were not required to discontinue their IOP medicinal product(s) until initiation of monotherapy with AZOPT. Among patients who were naive to IOP therapy (10 patients), the efficacy of AZOPT was similar to that seen previously in adults, with mean IOP reductions from baseline ranging up to 5 mmHg. Among patients who were on topical IOP-lowering medicinal products (22 patients), mean IOP increased slightly from baseline in the AZOPT group.

5.2 Pharmacokinetic properties

Following topical ocular administration, brinzolamide is absorbed into the systemic circulation. Due to its high affinity for CA-II, brinzolamide distributes extensively into the RBCs and exhibits a long halflife in whole blood (mean of approximately 24 weeks). In humans, the metabolite N-desethylbrinzolamide is formed, which also binds to CA and accumulates in RBCs. This metabolite binds mainly to CA-I in the presence of brinzolamide. In plasma, both brinzolamide and N-desethylbrinzolamide concentrations are low and generally below assay quantitation limits (<7.5 ng/ml).

Binding to plasma proteins is not extensive (about 60%). Brinzolamide is eliminated primarily by renal excretion (approximately 60%). About 20% of the dose has been accounted for in urine as metabolite. Brinzolamide and N-desethyl-brinzolamide are the predominant components in the urine along with trace levels of the N-desmethoxypropyl and O-desmethyl metabolites.

In an oral pharmacokinetic study, healthy volunteers received 1 mg capsules of brinzolamide twice daily for up to 32 weeks and RBC CA activity was measured to assess the degree of systemic CA inhibition.

Brinzolamide saturation of RBC CA-II was achieved within 4 weeks (RBC concentrations of approximately 20 μM). N-Desethyl-brinzolamide accumulated in RBCs to steady state within 20-28 weeks reaching concentrations ranging from 6-30 μM. The inhibition of total RBC CA activity at steady state was approximately 70-75%.

Subjects with moderate renal impairment (creatinine clearance of 30-60 ml/minute) were administered 1 mg of brinzolamide twice daily orally for up to 54 weeks. Brinzolamide RBC concentration ranged from about 20 to 40 μM by week 4 of treatment. At steady-state, brinzolamide and its metabolite RBC concentrations ranged from 22.0 to 46.1 and 17.1 to 88.6 μM, respectively.

N-desethyl-brinzolamide RBC concentrations increased and total RBC CA activity decreased with decreasing creatinine clearance but brinzolamide RBC concentrations and CA-II activity remained unchanged. In subjects with the highest degree of renal impairment inhibition of total CA activity was greater although it was inferior to 90% at steady-state.

In a topical ocular study, at steady-state, brinzolamide RBC concentrations were similar to those found in the oral study, but levels of N-desethyl-brinzolamide were lower. Carbonic anhydrase activity was approximately 40-70% of predose levels.

5.3 Preclinical safety data

Topical ocular administration of brinzolamide to rabbits for one to six months resulted in slight, statistically significant increases in corneal thickness when given at concentrations of 1%, 2% and 4%, four times a day; these changes were not observed in other species. Chronic administration of brinzolamide to rats at a dose level of 8 mg/kg/day (up to 250 times the recommended human ophthalmic dose) resulted in changes associated with the pharmacology of carbonic anhydrase inhibition (i.e., urine volume and electrolyte changes, slight differences in serum electrolytes).

A statistically significant increase in urinary bladder tumours was observed in female mice given brinzolamide 10 mg/kg/day (250 times the recommended human ophthalmic dose), orally, for 24 months. Dose-related proliferative changes in the urinary bladder were observed among female mice at 1, 3 and 10 mg/kg/day, and among males at 3 and 10 mg/kg/day. The elevated bladder tumour incidence, which was statistically significant, was primarily due to the increased incidence of a tumour considered unique to mice.

Developmental toxicity studies in rabbits with oral doses of brinzolamide of up to 6 mg/kg/day (125 times the recommended human ophthalmic dose) revealed no effect on foetal development despite significant maternal toxicity. Similar studies in rats resulted in slightly reduced ossification of skull and sternebrae of foetuses of dams receiving brinzolamide at doses of 18 mg/kg/day (375 times the recommended human ophthalmic dose), but not 6 mg/kg/day. These findings occurred at doses that caused metabolic acidosis with decreased body weight gain in dams and decreased foetal weights. Dose-related decreases in foetal weights were observed in pups of dams receiving brinzolamide orally ranging from a slight decrease (about 5-6%) at 2 mg/kg/day to nearly 14% at 18 mg/kg/day.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride,
mannitol,
carbomer 974P,
tyloxapol,
edetate disodium,
sodium chloride,
hydrochloric acid/sodium hydroxide (to adjust pH)
purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

2 years

4 weeks after first opening.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

5 and 10 ml opaque low density polyethylene bottles with polypropylene screw caps (droptainer).

The following pack sizes are available: outer cartons containing 1 x 5 ml, 3 x 5 ml and 1 x 10 ml bottles. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Alcon Laboratories (UK) Ltd.
Pentagon Park
Boundary Way
Hemel Hempstead
Herts HP2 7UD
United Kingdom.

8. MARKETING AUTHORISATION NUMBERS

EU/1/00/129/001-3

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9 March 2000
Date of last renewal: 9 March 2005

10. DATE OF REVISION OF THE TEXT

ANNEX II

A MANUFACTURING AUTHORISATION HOLDERS RESPONSIBLE FOR BATCH RELEASE

B CONDITIONS OF THE MARKETING AUTHORISATION

A. MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

S.A. Alcon-Couvreur N.V.,
Rijksweg 14,
B-2870 Puurs,
Belgium.

or

Alcon Cusí, S.A.,
Camil Fabra 58,
08320 El Masnou,
Barcelona,
Spain.

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OF THE MARKETING AUTHORISATION

- **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to medical prescription

- **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

Not applicable

- **OTHER CONDITIONS**

Pharmacovigilance system
The MAH must ensure that the system of pharmacovigilance, as described in version 4.0 presented in Module 1.8.1. of the Marketing Authorisation, is in place and functioning before and whilst the product is on the market.

Risk Management Plan
The MAH commits to performing the studies and additional pharmacovigilance activities detailed in the Pharmacovigilance Plan, as agreed in version 01 of the Risk Management Plan (RMP) presented in Module 1.8.2. of the Marketing Authorisation and any subsequent updates of the RMP agreed by the CHMP.

As per the CHMP Guideline on Risk Management Systems for medicinal products for human use, any updated RMP should be submitted at the same time as the following Periodic Safety Update Report (PSUR).

In addition, an updated RMP should be submitted

- When new information is received that may impact on the current Safety Specification, Pharmacovigilance Plan or risk minimisation activities

- Within 60 days of an important (pharmacovigilance or risk minimisation) milestone being reached

- At the request of the EMEA

PSURs to be submitted annually until the second Renewal application.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR SINGLE BOTTLE, 5 ml, 10 ml + CARTON FOR 3 x 5 ml BOTTLES

1. NAME OF THE MEDICINAL PRODUCT

AZOPT 10 mg/ml eye drops, suspension
Brinzolamide

2. STATEMENT OF ACTIVE SUBSTANCE

1 ml of suspension contains 10 mg of Brinzolamide

3. LIST OF EXCIPIENTS

Benzalkonium chloride, mannitol, carbomer 974P, tyloxapol, edetate disodium, sodium chloride, hydrochloric acid/sodium hydroxide (to adjust pH) and purified water. Contains benzalkonium chloride. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, suspension;
5 ml
10 ml
3 x 5ml

5. METHOD AND ROUTE OF ADMINISTRATION

Ocular use. Read the package leaflet before use. Shake well before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP: xx/xxxx
Discard four weeks after first opening.
Opened:
Opened (1):
Opened (2):
Opened (3):

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Alcon Laboratories (UK) Ltd.
Pentagon Park
Boundary Way
Hemel Hempstead
Herts, HP2 7UD
United Kingdom.

12. MARKETING AUTHORISATION NUMBERS

EU/1/00/129/001 1 x 5 ml
EU/1/00/129/002 1 x 10 ml
EU/1/00/129/003 3 x 5 ml

13. BATCH NUMBER

Lot.: xxxxx

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16 INFORMATION IN BRAILLE

Azopt.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
BOTTLE LABEL, 5 ml & 10 ml

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

AZOPT 10 mg/ml eye drops, suspension.
Brinzolamide 10 mg/ml. Ocular use.

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.
Discard 4 weeks after first opening.
Opened:

3. EXPIRY DATE

EXP: xx/xxxx

4. BATCH NUMBER

Lot.: xxxxx

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5 ml
10 ml

6 OTHER

B. PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

AZOPT 10 mg/ml eye drops, suspension
Brinzolamide

Read all of this leaflet carefully before you start using this medicine.
Keep this leaflet. You may need to read it again. If you have any further questions after reading it, please ask your doctor or your pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if their symptoms are the same as yours.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell you doctor or pharmacist.

In this leaflet

1. WHAT AZOPT IS AND WHAT IT IS USED FOR

AZOPT is one of a group of medicines for glaucoma called carbonic anhydrase inhibitors. It works by cutting down the production of liquid, which lowers the pressure in the eye. It may be used on its own or with other drops called beta-blockers or prostaglandin analogues, which also reduce pressure.

AZOPT eye drops are used to treat high pressure in the eye. This pressure can lead to an illness called **glaucoma.**

High pressure in the eye. Your eyeballs contain a clear, watery liquid which feeds the inside of the eye. Liquid is always emptying out of the eye, and more liquid is always being produced. If the eye fills up faster than it empties, the pressure inside the eye builds up. If it gets too high it can damage your sight.

2. BEFORE YOU USE AZOPT

Do not use AZOPT
- **if you have kidney problems.**

- **if you are allergic** to brinzolamide or any of the other ingredients.

- **if you are allergic to medicines called sulphonamides.** AZOPT may cause the same allergy.

- **if you have a condition called hyperchloraemic acidosis** (too much acidity in your blood).

- Ask your doctor for advice .

Take special care with AZOPT

Talk to your doctor
- **if you have liver problems.**
- **if you have dry eyes or cornea problems.** Talk to your doctor.
- **if you wear soft contact lenses.** Don't use the drops with your lenses in. Wait 15 minutes after using the drops before putting your lenses back in to your eyes. A preservative in AZOPT (benzalkonium chloride) may cause eye irritation and is also known to discolour soft contact lenses.

AZOPT is not to be used by people under 18 of years of age unless advised by your doctor.

Using other medicines

If you are taking another carbonic anhydrase inhibitor (acetazolamide or dorzolamide, see section 1 WHAT AZOPT IS AND WHAT IT IS USED FOR), talk to your doctor. Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding

If you are pregnant, or might get pregnant, talk to your doctor before you use AZOPT.
If you are breast-feeding, don't use AZOPT; it may get into your milk.

Ask your doctor or pharmacist for advice before taking any medicine

Driving or using machines
You may find that your vision is blurred for a time just after you use AZOPT. Some people have found themselves sleepy or dizzy when taking AZOPT. Do not drive or use machines until this has worn off.

Important information about some of the ingredients of AZOPT
If you wear soft contact lenses. Do not use the drops while your contact lenses are in your eyes. Wait 15 minutes after using the eye drops before putting your lenses back into your eyes. A preservative in AZOPT (benzalkonium chloride) can affect soft lenses.

3. HOW TO USE AZOPT

Always use AZOPT exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

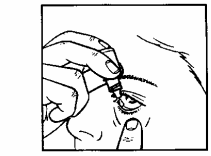
The usual dose is

1 drop in the eye or eyes, twice a day-morning and night.
Use this much unless your doctor told you to do something different. Only use AZOPT in both eyes if your doctor told you to. Take it for as long as your doctor told you to.

Only use AZOPT for dropping in your eyes.
Turn the page for more advice

Now turn over>

3. HOW TO USE AZOPT (*continued)*



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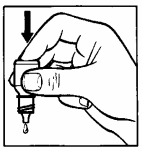

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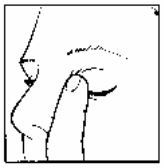

3

How much to use
< see side 1

- Get the AZOPT bottle and a mirror
- Wash your hands
- Shake the bottle and twist off the cap
- Hold the bottle, pointing down, between your thumb and middle finger
- Tilt your head back. Pull down your eyelid with a clean finger, until there is a 'pocket' between the eyelid and your eye. The drop will go in here (picture 1)
- Bring the bottle tip close to the eye. Use the mirror if it helps
- **Don't touch your eye or eyelid, surrounding areas or other surfaces with the dropper.** It could infect the drops
- Gently press on the base of the bottle to release one drop of AZOPT at a time.
- **Don't squeeze the bottle:** it is designed so that a gentle press on the bottom is all that it needs (picture 2)
- After using AZOPT, press a finger to the corner of your eye, by the nose (picture 3) . This helps to stop AZOPT getting into the rest of the body.
- If you take drops in both eyes, repeat the steps for your other eye.
- Put the bottle cap back on firmly immediately after use
- Use up one bottle before opening the next bottle.

If a drop misses your eye, try again.

If you get too much in your eyes, rinse it all out with warm water. Don't put in any more drops until it's time for your next regular dose.

If you forget to use AZOPT, use a single drop as soon as you remember, and then go back to your regular routine. **Do not** use a double dose to make up.

If you stop using AZOPT without speaking to your doctor, the pressure in your eye will not be controlled which could lead to loss of sight.

If you are using other eye drops, leave at least 5 minutes between putting in AZOPT and the other drops.

4. POSSIBLE SIDE EFFECTS

Like all medicines, AZOPT can cause side effects, although not everyone gets them.

You can usually carry on taking the drops, unless the effects are serious

Common side effects
(1 to 10 users in 100)
Effects in the eye: blurred vision, eye irritation, eye pain, eye discharge, itchy eye, dry eye, abnormal eye sensation, redness of the eye, eyelid itching, redness, or swelling.

General side effects: bad taste, headache, dry mouth

Uncommon side effects
(1 to 10 users in 1,000)
Effects in the eye: increased pressure in eye, damage to the optic nerve, abnormal, double, or reduced vision, sensitivity to light, inflammation or infection of the conjunctiva, eye allergy, eye swelling, corneal disorder, inflammation of the eyelid glands, decreased eye sensation, growth on surface of eye, increased pigmentation of the eye, tired eyes, eyelid crusting, or increased tear production.

General side effects: decreased or irregular heart rate, reduced heart function, chest pain, asthma, difficulty breathing, shortness of breath, decreased red blood cell count in blood, increased chlorine level in blood, dizziness, drowsiness, difficulty with memory, depression, difficulty sleeping, nervousness, irritability, fatigue, generalized weakness, feeling abnormal, pain, shaking, ringing in ears, decreased sex drive, male sexual difficulty, cold symptoms, chest congestion, cough, sinus infection, throat irritation, abnormal or decreased sensation in mouth, inflammation of the lining of the oesophagus, abdominal pain, nausea, upset stomach, frequent bowel movements, diarrhoea, intestinal gas, digestive disorder, kidney pain, muscle pain, muscle spasms, back pain, nose bleeds, dry nose, runny nose, stuffy nose, sneezing, rash, abnormal skin sensation, itching, loss of hair

Additional side effects that have been reported include:

Effects in the eye: eyelid abnormality, decreased growth or number of eyelashes

General side effects: increased allergic symptoms, increased blood pressure, increased heart rate, abnormal liver blood tests, vomiting, frequent urination, swelling of the extremities, decreased sensation, decreased taste sensation, joint pain, pain in extremity, skin redness, inflammation, or itching

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE AZOPT

Keep out of the reach and sight of children.

Do not use AZOPT after the expiry date which is stated on the bottle and box after "EXP". The expiry date refers to the last day of the month.

This medicine does not require any special storage conditions.

You must throw away a bottle four weeks after you first opened it, to prevent infections. Write down the date you opened each bottle in the space below and in the space on the bottle label and box. For a pack containing a single bottle, write only one date.

Opened (1):
Opened (2):
Opened (3):

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help protect the environment.

6 FURTHER INFORMATION

What AZOPT contains

The active substance is brinzolamide 10 mg/ml.

The other ingredients are: benzalkonium chloride, carbomer 974P, edetate disodium, mannitol, purified water, sodium chloride, tyloxapol. Tiny amounts of hydrochloric acid or sodium hydroxide are added to keep acidity levels (pH levels) normal.

What AZOPT looks like and the contents of the pack
AZOPT is a milky liquid (a suspension) supplied in a pack containing a 5 ml or a 10 ml plastic (droptainer) bottle with a screw cap, or in a pack containing three 5 ml plastic (droptainer) bottles with screw caps. Not all pack sizes may be marketed.

The marketing authorisation holder	**Manufacturer**	**Manufacturer**
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This leaflet was last approved on XXXXX

Detailed information on this product is available on the website of the European Medicines Agency (EMEA) http://www.emea.europa.eu